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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,251	03/10/1999	DAVID JOHN KING	CARP-0067	9023

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	16

DATE MAILED: 03/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/214,251	KING ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 9-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The request filed on 1/7/02 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/214251 is acceptable and a RCE has been established. Claim 1 has been cancelled and claim 12 has been added. Claims 5, 9, 10-12 are pending and are currently under prosecution. An action on the RCE follows.

2. The text of those sections of Title 35 U.S.C. code not included in this office action can be foound in a prior Office Action

3. The following Office Action contains some NEW GROUNDS of rejection.

Rejections Withdrawn

4. The rejection of claims under 35 U.S.C. 102(e) as being anticipated by Griffiths et al (U.S. Patent 5,670,132, filed 9/20/94) is withdrawn in view of the amendments to the claims and arguments presented.

5. The rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al (U. S. Patent 5,670,132) and further in view of Goodson et al (Bio/Technology 8:343-346, 1990, IDS # 8) or Woghiren et al (Bioconjugate Chem. 4:314-318, 1993) is withdrawn in view of the amendments to the claims and arguments presented.

The following are some NEW GROUNDS of rejections

Claim Rejections - 35 USC § 112

6. Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 9-12 are indefinite for reciting "poly(ethylene glycol), poly(ethylene glycol)" because the exact meaning of the phrase is not clear. It is not clear if the second occurrence of "poly(ethylene glycol) was a typographical error or if some other form of the polymer is indicated.

b. Claim 12 recites the limitation "said antigen-binding fragment" in line 2 of claims 12. There is insufficient antecedent basis for this limitation in the claim.

c. Claim 12 recites the limitation "said hinge region" in line 10 of claim 12. There is insufficient antecedent basis for this limitation in the claim.

d. Claim 12 recites the limitation "said polymer" in line 11 of claim 12. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 5, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Zapata et al (FASEB J. 9:A1479, 1995).

The claims recite a polymer modified monovalent antibody fragment which is a Fab' wherein the CH1 is extended to provide a hinge that comprises not more than one cysteine and wherein not more than one polymer of a derivative of methoxy(polyethylene glycol) is linked to the cysteine residue in the hinge region.

Zapata et al teach a Fab' fragment which contains a single cysteine in the hinge region and coupling of monomethoxypoly(ethylene glycol) to the cysteine.

Claim Rejections - 35 USC § 103

9. Claims 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zapata et al [a] (FASEB J. 9:A1479, 1995) as applied to claims 5, 11-12 above, and further in view of Zapata [b] (U. S. Patent 6,214,984, continuation date of 4/20/95).

Claims 5, 11-12 have been described supra. Claims 9-10 recite wherein the antibody fragment is covalently attached to one effector or reporter molecule and a composition comprising the antibody and a carrier.

Zapata et al has been described supra. Zapata et al [a] also teach the antibody is an anti-CD18 antibody. Zapata et al [a] does not specifically teach a composition with a carrier or a fragment with an effector or reporter molecule. These deficiencies are made up for in the teachings of Zapata [b].

Zapata [b] teach a Fab' fragment that has been engineered to have one cysteine in the hinge (see column 17, lines 35-43) and the antibody fragment can be labeled with a reporter molecule (see column 14, lines 29-37) and compositions comprising carriers (see column 15, lines 9-36).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antigen binding fragment with PEG as taught by Zapata et al [a] and label the fragment and produce compositions comprising a carrier and the antibody as taught by Zapata [b].

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antigen binding fragment with PEG as taught by Zapata et al [a] and label the fragment and produce compositions comprising a carrier and the antibody as taught by Zapata [b] because Zapata et al [a] teach "the ability to modify the clearance rate of an antibody Fab' fragment by attaching a single MePEG moiety at a unique site, without affecting antigen binding, increases significantly the potential therapeutic value of this type of molecule". In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antigen binding fragment with PEG as taught by Zapata et al [a] and label the fragment and produce compositions comprising a carrier and the antibody as taught by Zapata [b] because Zapata [b] teach therapeutic applications for CD18 with anti-CD18 antibody fragments and these fragments can be labeled with a detectable moiety and the antibodies can be used in therapeutic applications when combined with acceptable carriers (see column 14 and column 15). In addition, it would have been obvious to one of skill in the art to label antibody fragments for detection or therapy and to formulate compositions comprising a carrier for therapeutic applications.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

10. Claims 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al (U. S. Patent 5,853,723, filed 9/20/96) and further in view of Bodmer et al (WO 89/01974, published 3/9/89).

The claims have been described supra.

Jacobs et al teach methoxy-PEG coupled to a Fab' fragment through a hinge cysteine residue and compositions comprising excipients and the fragments can be labeled (see column 7, lines 25-41, 62-67, column 8, lines 35-40, and Figure 1 and 2). Jacobs et al does not specifically teach the Fab' with a single cysteine residue in the hinge. This deficiency is made up for in the teachings of Bodmer et al.

Bodmer et al teach reducing the cysteines in the hinge to one for the purpose of attaching other molecules (see page 7) and to reduce the complexity of subsequent chemical additions at the hinge (see page 10, Example 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have reduced the number of cysteine residues in the hinge to one as taught by Bodmer et al and produce a Fab'-PEG antigen binding fragment as taught by Jacobs et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have reduced the number of cysteine residues in the hinge to one as taught by Bodmer et al and produce a Fab'-PEG antigen binding fragment as taught by Jacobs et al because Jacobs et al teach the polymer provides a

hydration shell around the monoclonal antibody or fragment for inhibiting immune recognition (see column 6, lines 5-10). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have reduced the number of cysteine residues in the hinge to one as taught by Bodmer et al and produce a Fab'-PEG antigen binding fragment as taught by Jacobs et al because Bodmer et al teach by reducing the cysteine residues in the hinge to one this reduces the complexity of subsequent chemical additions to the hinge. In addition, it would have been obvious to one of skill in the art to label antibody fragments for detection or therapy and to formulate compositions comprising a carrier for therapeutic applications as which are taught by Jacobs et al

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusions

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879